

CLAIM AMENDMENTS

1. (currently amended): A method for modifying the nature of the extender unit substrate used by a first modular polyketide synthase (PKS) encoded by a first nucleic acid which method comprises:

excising by restriction enzyme reaction a first region consisting essentially of a nucleotide sequence encoding an acyltransferase (AT) domain of said first PKS-encoding nucleic acid and inserting ligating said excised first region into a second AT-domain-encoding region of a second PKS-encoding nucleic acid from which a nucleotide sequence consisting essentially of said second AT domain-encoding region has been excised by restriction enzyme reaction,

wherein the extender unit specificity of said first region is different from the extender unit specificity of the second region, and wherein the modular PKS from which the first extender unit is excised is not the modular PKS from which the second extender unit is obtained,

to produce nucleic acid encoding a PKS which uses a different extender unit substrate from the first PKS.

2. (original): The method of claim 1 wherein the first or second PKS is from *Saccharopolyspora erythraea*.

3. (original): The method of claim 1 wherein the first or second PKS is from *Streptomyces*.

4. (original): The method of claim 3 wherein the *Streptomyces* is *Streptomyces hygroscopicus*.

5. (original): The method of claim 1 wherein the first PKS or second PKS is selected from the group consisting of erythromycin, rapamycin, avermectin, FK-506, and tylosin.

6. (canceled)

7. (currently amended): A method for modifying the nature of the extender unit substrate used by a first modular PKS encoded by a first nucleic acid which method comprises:

effecting *in vivo* recombination, wherein said recombination is from a donor plasmid comprising said first nucleic acid comprising said first AT domain-encoding region of a first PKS-encoding nucleic acid framed by a first pair of flanking sequences,

into a recipient plasmid comprising a second nucleic acid encoding a second PKS wherein in said recipient plasmid a second AT domain-encoding region in a second PKS encoding nucleic acid is framed by a second pair of flanking sequences which are homologous to said first pair of flanking sequences,

wherein the extender unit specificity of said first region is different from the extender unit specificity of the second region

to produce nucleic acid encoding a PKS which uses a different extender unit substrate from the first PKS,

wherein said donor and recipient plasmids comprise different selectable markers, and
wherein said donor plasmid is temperature sensitive.

8-9. (canceled)

10. (original): The method of claim 7 wherein the first or second PKS is from *Saccharopolyspora erythraea*.

11. (original): The method of claim 7 wherein the first or second PKS is from *Streptomyces*.

12. (original): The method of claim 11 wherein the *Streptomyces* is *Streptomyces hygroscopicus*.

13. (original): The method of claim 7 wherein the first PKS or second PKS is selected from the group consisting of erythromycin, rapamycin, avermectin, FK-506, and tylosin.

14-30. (canceled)

31. (new): The method of claim 1 wherein at least one restriction site acted on by at least one restriction enzyme is inserted by PCR amplification.